

Statement from Dr. Blake Bextine, DARPA Program Manager for Insect Allies

As the DARPA program manager for Insect Allies, I appreciate the thought that went into the critique of the program presented in *Science*, though I disagree with its conclusions. Technologies dealing with food security and gene editing certainly do have a higher bar than most for transparency, research ethics, and regulatory engagement, and I believe Insect Allies meets that raised standard. DARPA structured Insect Allies as a university-led, fundamental research program, and has invited in representatives from U.S. regulatory agencies from the very beginning of the program to offer perspectives and learn about the work. The researchers working with DARPA are free to publish their results, encouraged to discuss their efforts, and coordinate with regulatory agencies to facilitate the transition of their technologies from laboratory demonstrations to—someday in the future—powerful new tools that can bolster the toolkit for responding to fast-moving or unanticipated threats to the global food supply.

DARPA created Insect Allies to provide new capabilities to protect the United States, specifically the ability to respond rapidly to threats to the food supply. A wide range of threats may jeopardize food security, including intentional attack by an adversary, natural pathogens, and pests, as well as by environmental phenomena such as drought and flooding. Insect Allies aims to develop scalable, readily deployable, and generalizable countermeasures against potential natural and engineered threats to mature crops. The program is devising technologies to engineer and deliver these targeted therapies on relevant timescales—that is, within a single growing season. To do so, Insect Allies researchers are building on natural, efficient, and highly specific plant virus and insect vector delivery systems to transfer modified, protective genes to plants. Since the start of the program, Insect Allies teams with expertise in molecular and synthetic biology have demonstrated mounting technical breakthroughs that are providing foundational knowledge in plant virus gene editing and disease vector biology from which the program will continue to build.

State-of-the-art methods and technologies for protecting staple crops, and especially mature plants, are not up to the challenge of responding quickly and at scale to the most severe threats. The authors of the *Science* piece point to spraying technologies as an effective solution, but their argument overlooks some of the key elements that Insect Allies aims to address. Namely, many existing methods for protecting crops are inefficient, expensive, imprecise, or destructive to plants, may require significant infrastructure, and often provide only limited efficacy. Sprayed treatments are impractical for introducing genetic modifications on a large scale and potentially infeasible if the spraying technology does not access the necessary tissues with specificity. Meanwhile, traditional selective breeding methods for introducing protective traits into plants require years to propagate, nowhere near the speed required to prevent a fast-moving threat from developing into a crisis.

DARPA made the move into agriculture for two reasons. First, the stability of our domestic agricultural sector represents a critical, but often under-appreciated element of national security. If DARPA can deliver technologies that keep the U.S. resilient in the face of threats, we preserve stability and readiness at home and diminish a source of instability abroad. Second, DARPA has a unique charter to pursue revolutionary and technologically high-risk projects that go well beyond the incremental advances typical of many other research and development organizations. DARPA would never fund the next generation of aerial spraying technology; that is the role of industry and other research funders. Instead, we reach for fundamentally new ways of delivering more precise, efficacious treatments through systems that can be readily adapted to confront a range of potential threats.

Part of the DARPA model is to demonstrate proof of concept and remove degrees of risk from a new technology to facilitate its eventual transition to an end user. For Insect Allies, we scheduled a four-year program of research that concludes with demonstrations inside large, biosecure greenhouses. At no point in the program is DARPA funding open release of Insect Allies systems. Regulatory approval has been a part of the program since its inception as it would be necessary for any eventual realization of the technology. Interactions with regulators have provided comprehensive and alternative perspectives to the DARPA-funded efforts, and updates from our researchers help to inform the evolution of new guidelines and policies by those very same regulators. Representatives from the U.S. Food and Drug Administration, Environmental Protection Agency, and Department of Agriculture's Animal and Plant Health Inspection Service (Biotechnology Regulatory Services and Plant Health) and Agricultural Research Service participate in Insect Allies meetings and program reviews. One illustration of this dynamic between DARPA, researcher, and regulator is the criticality of building in safeguards and limitations to Insect Allies technology. Every performer in the program is required to include at least three independent kill switches in their systems to shut down functionality of the technology. This is in addition to bio-containment requirements in the active program.

The stakeholder interactions mentioned above are ongoing, and I offer a few examples of participants and their contributions:

- Dr. Jacqueline Fletcher of the National Institute for Microbial Forensics & Food and Agricultural Biosecurity at Oklahoma State University and Dr. Sonny Ramaswamy, then director of USDA's National Institute of Food and Agriculture, both spoke at the Insect Allies Proposers Day on November 18, 2016.
- Dr. Richard Murray, Thomas E. and Doris Everhart Professor of Control & Dynamical Systems and Bioengineering at the California Institute of Technology, presented on a National Academies report titled "Preparing for Future Products of Biotechnology" at the Insect Allies kickoff meeting on August 14, 2017.
- Georg Jander, principal investigator for the Insect Allies team led by The Boyce Thompson Institute, presented results and perspective to the Trilateral Technical Working Group (TTWG) on May 31, 2018. The TTWG is composed of agricultural biotechnology regulators from the United States, Canada, and Mexico.
- The Insect Allies program benefits from the input of independent advisors on legal, ethical, environmental, dual-use, and responsible innovation (LEEDR) topics. These advisors include: Dr. Richard Murray (Caltech); Dr. Jim Stack, Fellow, Biosecurity Research Institute/Professor, Department of Plant Pathology/Director, Great Plains Diagnostic Network, Kansas State University; and Dr. Paul Thompson, W. K. Kellogg Chair in Agricultural Food and Community Ethic, Michigan State University.

Emerging biotechnologies—and especially the cutting-edge research being performed on Insect Allies—are pushing science into new territories. DARPA is proud to be taking a proactive role in working with stakeholders to inform a new framework for considering how the benefits of these technologies can be most safely realized.